



Therapeutic Class ReviewSM

Antidotes – Prussian blue (RadiogardaseTM)

December 2007

New Product for Review:

Prussian blue (RadiogardaseTM)
[Heyltx Corporation]

Dossier Provided by Manufacturer: No

Dossier Evaluation: N/A

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Available Therapeutic Alternatives:

- Prussian blue has been the standard of care for cesium and thallium contamination since the 1960s. Other treatments include supportive measures. Bone marrow transplants cannot occur while contamination is present.

Issues

- Is there useful evidence to demonstrate the safety and efficacy of Prussian blue (Radiogardase)?
- Does Prussian blue (Radiogardase) address an unmet medical need?
- Are there any considerations with Prussian blue (Radiogardase) specific to age, gender, or race?

Executive Summary

- Prussian blue (Radiogardase) is the only FDA approved treatment for ¹³⁷Cs contamination and thallium poisoning. It was approved in 2003, based on an accumulation of data from published monographs, small retrospective studies and the feeling that Prussian blue (Radiogardase) fulfilled an unmet medical need.
- Cesium-137 (¹³⁷Cs) is a radioactive material used in equipment found in hospitals, factories, construction sites and food processing plants. It is most commonly available as a dispersed powder, which can also be used in a radiological dispersion device (dirty bomb) for purposes of biological warfare.
- Thallium was formerly used as a rat poison, though most common cases of human ingestion are usually cases of attempted homicide or suicide.
- The FDA approved Prussian blue (Radiogardase) in an effort to make a regulated product available in case of bioterrorism, while ensuring product quality.

- Marketing of Prussian blue (Radiogardase) began in 2007. The manufacturer emphasizes the importance of stockpiling Prussian blue (Radiogardase) for handling the aftermath of potential ¹³⁷Cs dirty bomb attacks. Distribution is limited to one specialty pharmacy at this time.
- Prussian blue (Radiogardase) appears to increase fecal elimination of ¹³⁷Cs which reduces the whole body half-life. This leads to decreased whole body radiation exposure which is thought to reduce the risk of bone marrow suppression and radiation induced cancer.
- The long-term safety of Prussian blue (Radiogardase) is unknown. However, this must be balanced with the potentially deadly effects of ¹³⁷Cs contamination and thallium poisoning.
- Over-utilization of Prussian blue (Radiogardase) is not likely, as it does not appear to be efficacious for excretion of other radioisotopes.
- Prussian blue (Radiogardase) is recognized by the FDA as a new molecular entity which addresses an unmet medical need.

Evidence

- Prospective trials have not been performed to demonstrate the safety and efficacy of Prussian blue (Radiogardase) in humans.

Consideration in subpopulations

- There is minimal experience with the use of Prussian blue (Radiogardase) in pediatric populations.
- Prussian blue (Radiogardase) has not been studied in pregnancy. However, the risk of toxicity from untreated ¹³⁷Cs or thallium exposure must be balanced with the potential risk of toxicity associated with Prussian blue (Radiogardase).

Conclusion

Prussian blue (Radiogardase) is preferred/formulary because:

- The benefits of treating patients exposed to ¹³⁷Cs or thallium are likely to outweigh the risks of no treatment.
- This product meets an unmet medical need.
- There is low risk of over-utilization.

Products

Drug Products	FDA approval ^a	Patent expiration ^c	FDA approved indications	Usual Dose/Route	Cost ^b
Prussian blue (Radiogardase TM) ¹	10/2003	10/2008	Enhancement of excretion of ¹³⁷ Cs and thallium in patients with known or suspected internal contamination.	3 g p.o. t.i.d. (adults and adolescents) 1 g p.o. t.i.d. (children 4 – 12)	\$1,440 (adults) \$480 (children)

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank as of October 2007 for 1 month of therapy.

^c Based on patents listed in the Orange Book as of 10/01/2007.

References

1. Radiogardase™ (Prussian blue) Prescribing Information. Heyltex Corporation: Katy, Texas; 2007.
2. The Radiological Accident in Goiania: Report of the Review Meeting on the Goiania Accident in Rio de Janeiro 18 – 22 July 1988. International Atomic Energy Agency Vienna 1988 ISBN 92-0-129088-8.
3. Drugs@FDA [page on the internet]. Label, approval history and review for Radiogardase. Available at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search DrugDetails>.
4. Radiation disasters and children. *Pediatrics* 2003 Jun;111(6 Pt 1):1455-66.
5. Hoffman RS. Thallium toxicity and the role of Prussian blue in therapy. *Toxicol Rev* 2003;22(1):29 – 40.